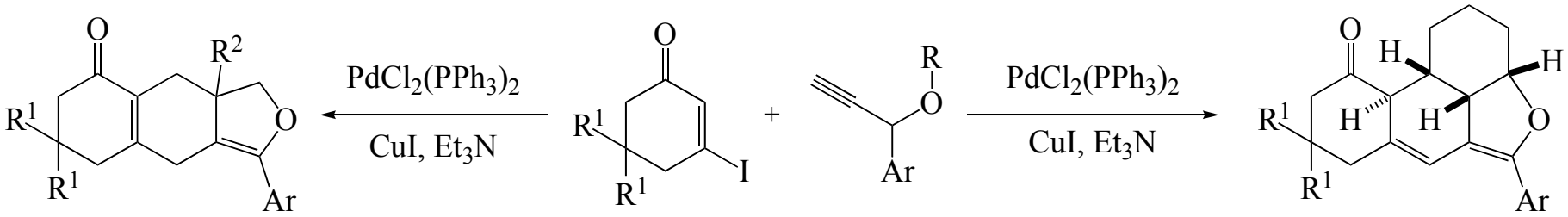
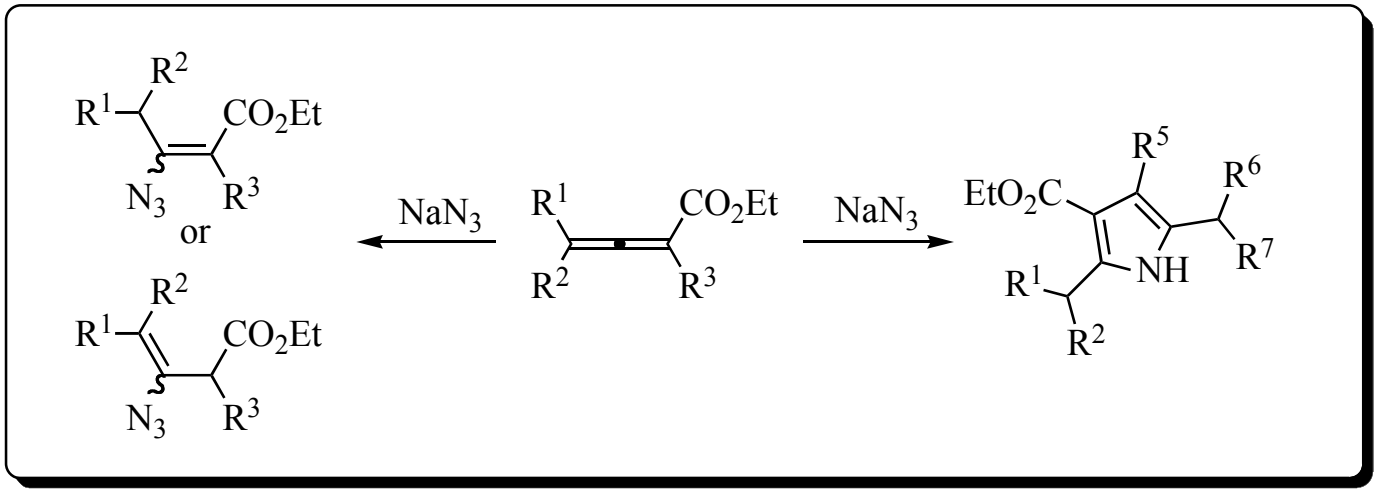
Pd-Catalyzed Sequential Reactions via Allene Intermediate for the Synthesis of Polycyclic Frameworks Containing 2,3-Dihydrofuran Units

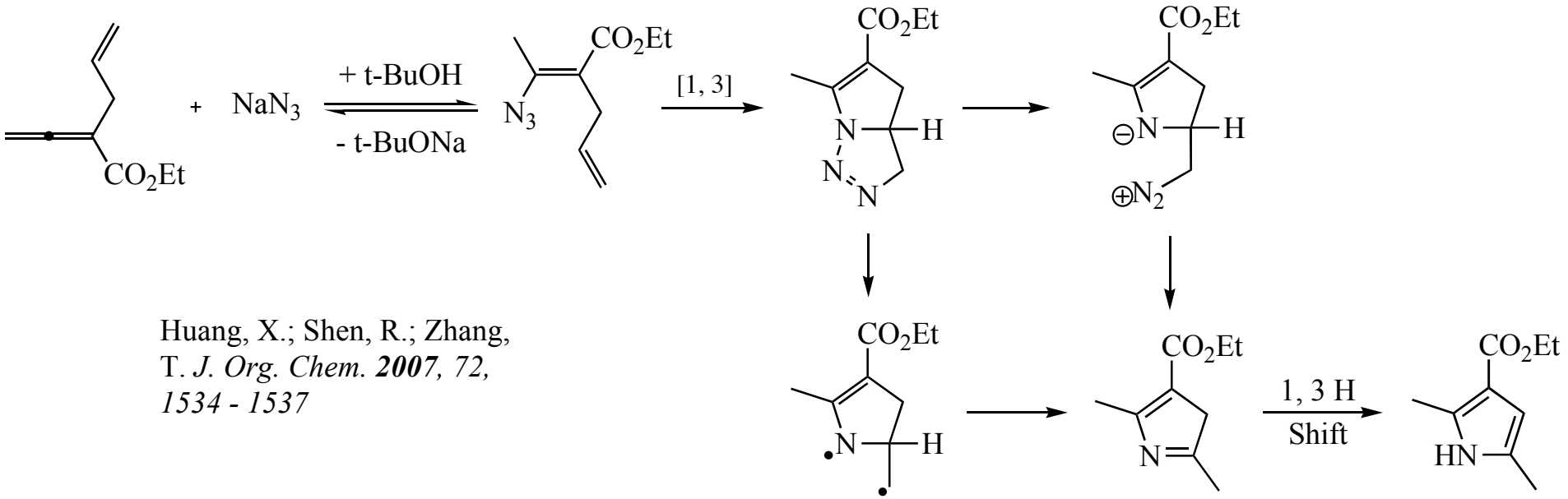
Shen, R.; Huang, X. *Org. Lett*. **2008**, ASAP



Eric E. Buck
Current Literature
July 19, 2008

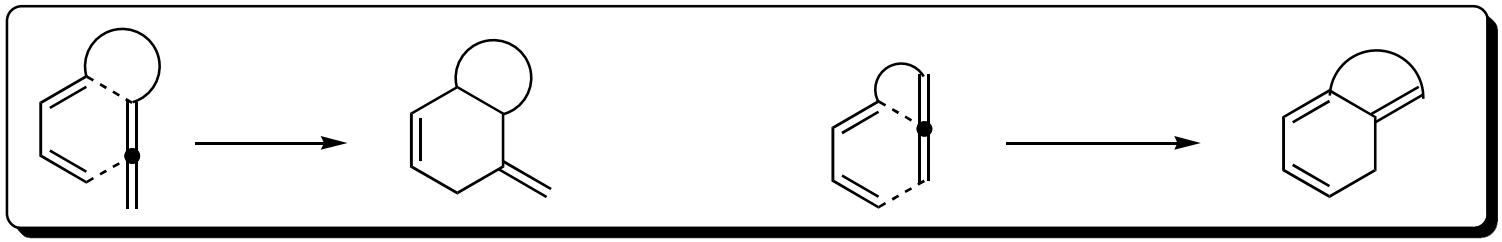
Previous work in the Huang group

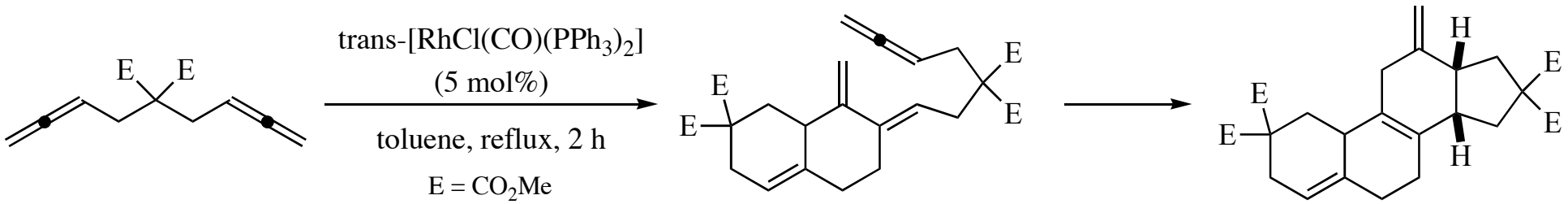




Huang, X.; Shen, R.; Zhang, T. *J. Org. Chem.* ***2007****, 72, 1534 - 1537*

Intramolecular [4 + 2] cycloadditions of allenes





Ma, S.; Lu, P.; Lu, L.; Hou, H.; Wei, J.; He, Q.; Gu, Z.; Jiang, X.; Jin, X. *Angew. Chem. Int. Ed.* ***2005****, 44, 5275 - 5278*

69 %

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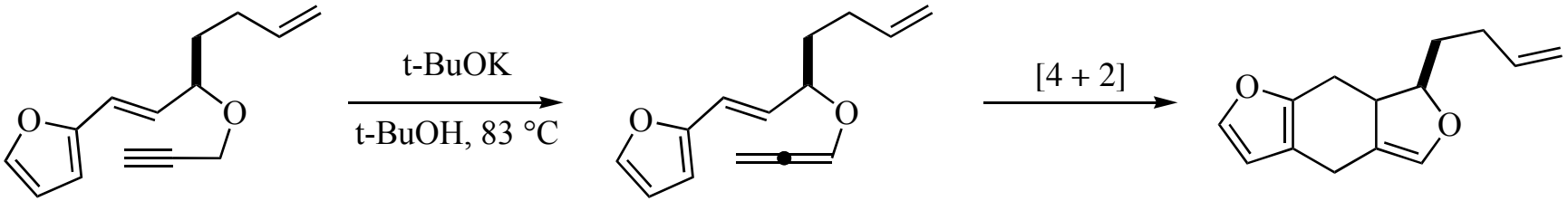
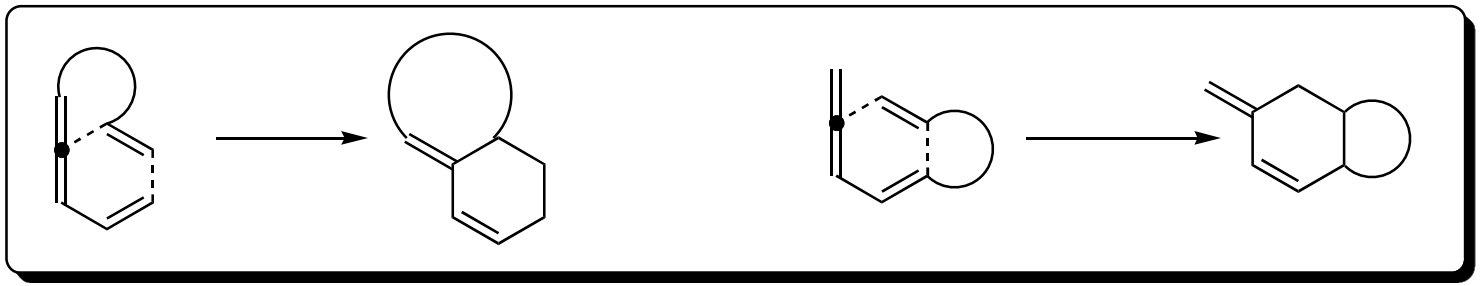
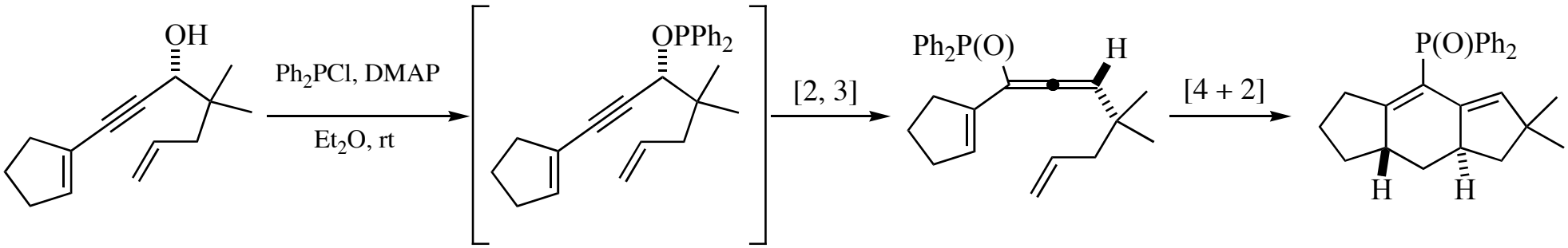


Intramolecular [4 + 2] cycloadditions of ene - allenes





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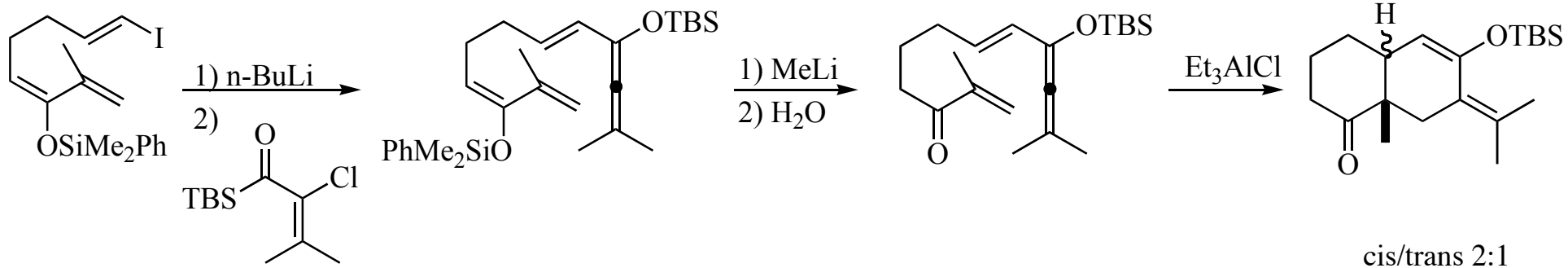
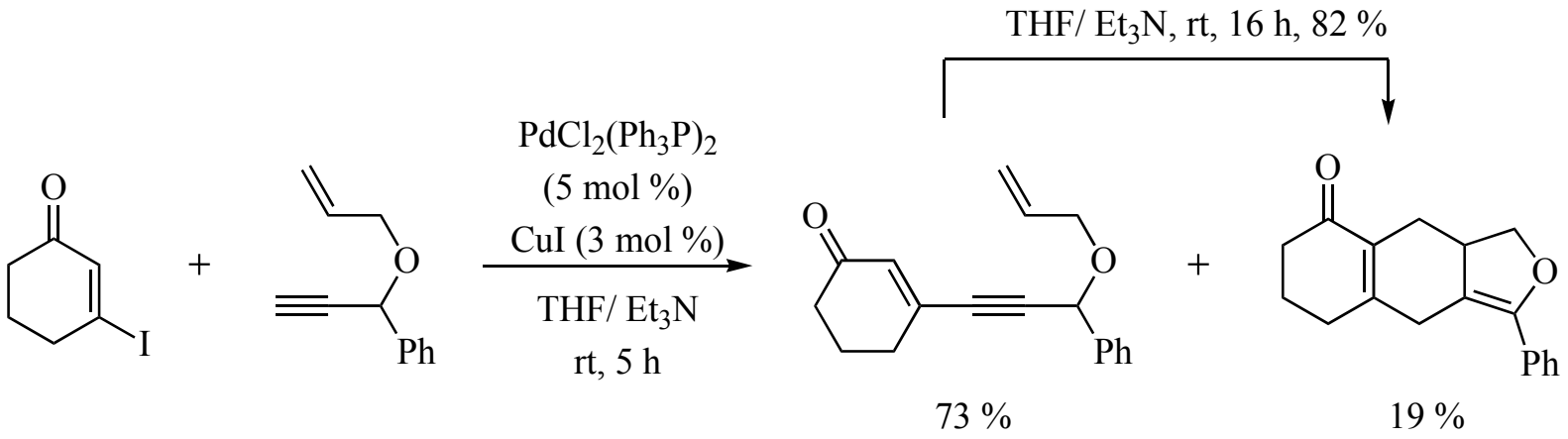


cis/trans 2:1

Title paper: The initial study and variation of the amine base



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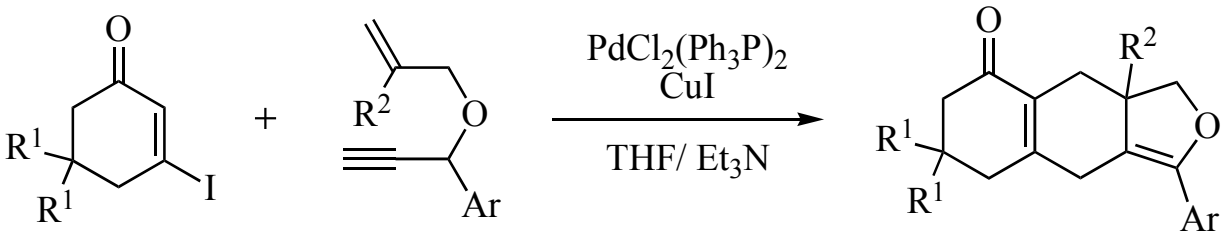
Thorand, S.; Krause, N. *J. Org. Chem*. **1998**, 63, 8551 - 8553

Improved procedures for the Sonogashira coupling

entry	solvent	base	yield (%)
1	THF	Et_3N	75
2	THF	$(n\text{-}C_4H_9)_3N$	75
3	THF	Et_2NH	-
4	THF	pyrrolidine	-
5	THF	$i\text{-}Pr_2NH$	-
6	THF	TMEDA	68
7	Toluene	Et_3N	74
8	MeCN	Et_3N	71

Synthesis of tricycles and variation of Aromatic functionality

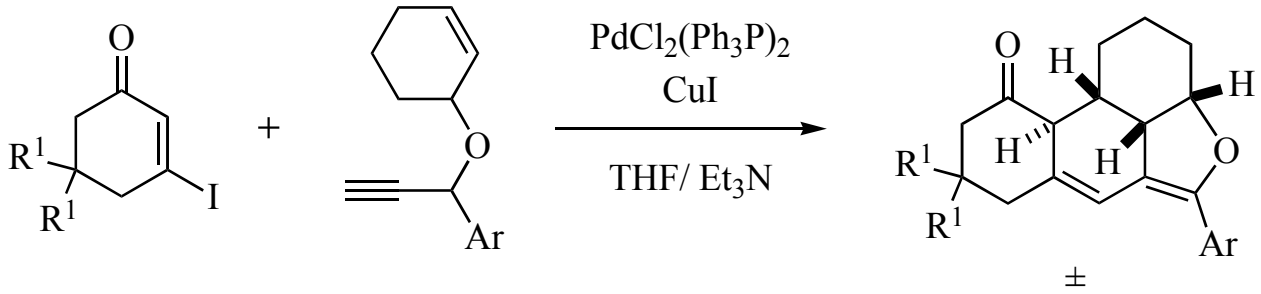


entry	R^1	R^2	Ar	yield (%)
1	Me	H	C_6H_5	73
2	Me	H	p-MeC_6H_4	80
3	Me	H	o-BrC_6H_4	68
4	Me	H	p-FC_6H_4	79
5	H	H	o-BrC_6H_4	65
6	H	H	p-MeC_6H_4	76
7	Me	H	m-BrC_6H_4	81
8	Me	H	o-$MeOC_6H_4$	71

entry	R^1	R^2	Ar	yield (%)
9	Me	Me	C_6H_5	85
10	H	Me	C_6H_5	81
11	Me	Me	p-FC_6H_4	85
12	H	Me	p-MeC_6H_4	75
13	H	Me	p-FC_6H_4	80

Shen, R.; Huang, X. *Org. Lett*. **2008**, ASAP

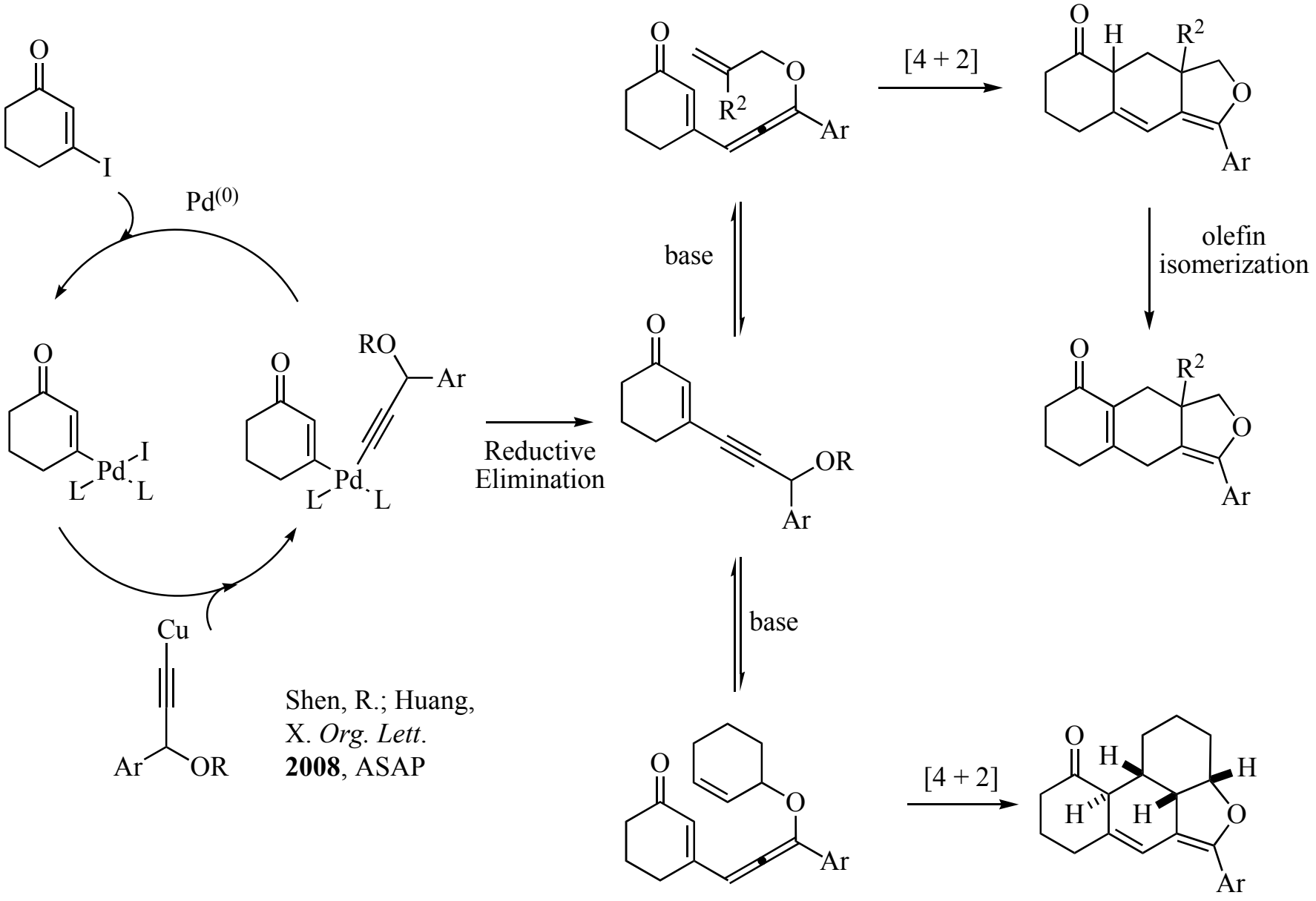
Synthesis of tetracycles



entry	R^1	Ar	time (h)	yield (%)
1	H	C_6H_5	18	55 (46)
2	Me	p-MeC_6H_4	24	63
3	H	p-MeC_6H_4	20	58
4	H	p-ClC_6H_4	16	63
5	H	p-FC_6H_4	10	71
6	Me	p-FC_6H_4	10	76
7	Me	o-BrC_6H_4	24 h or 18 h	-

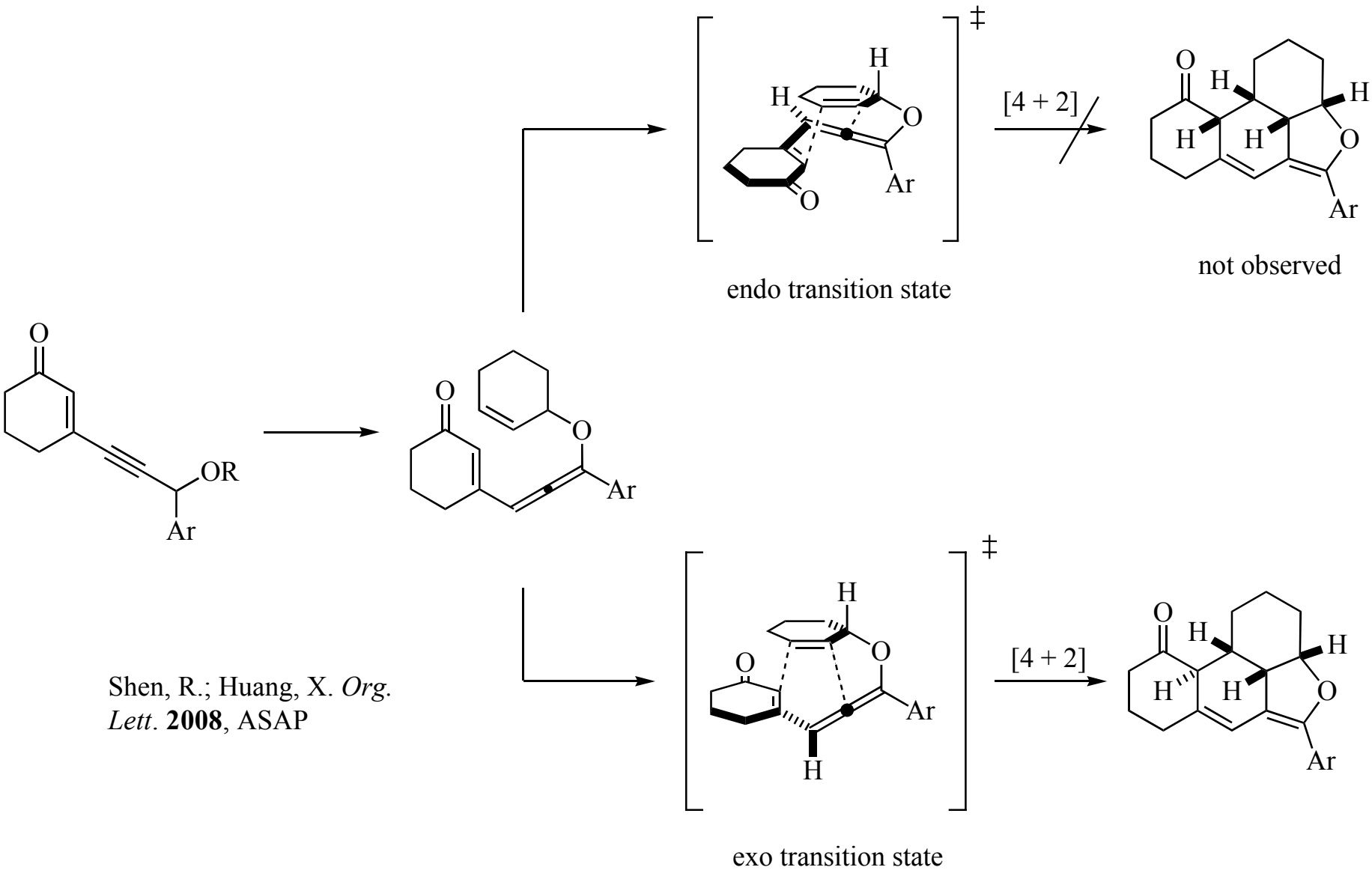
Shen, R.; Huang, X.
Org. Lett. **2008**, ASAP

Proposed Mechanism



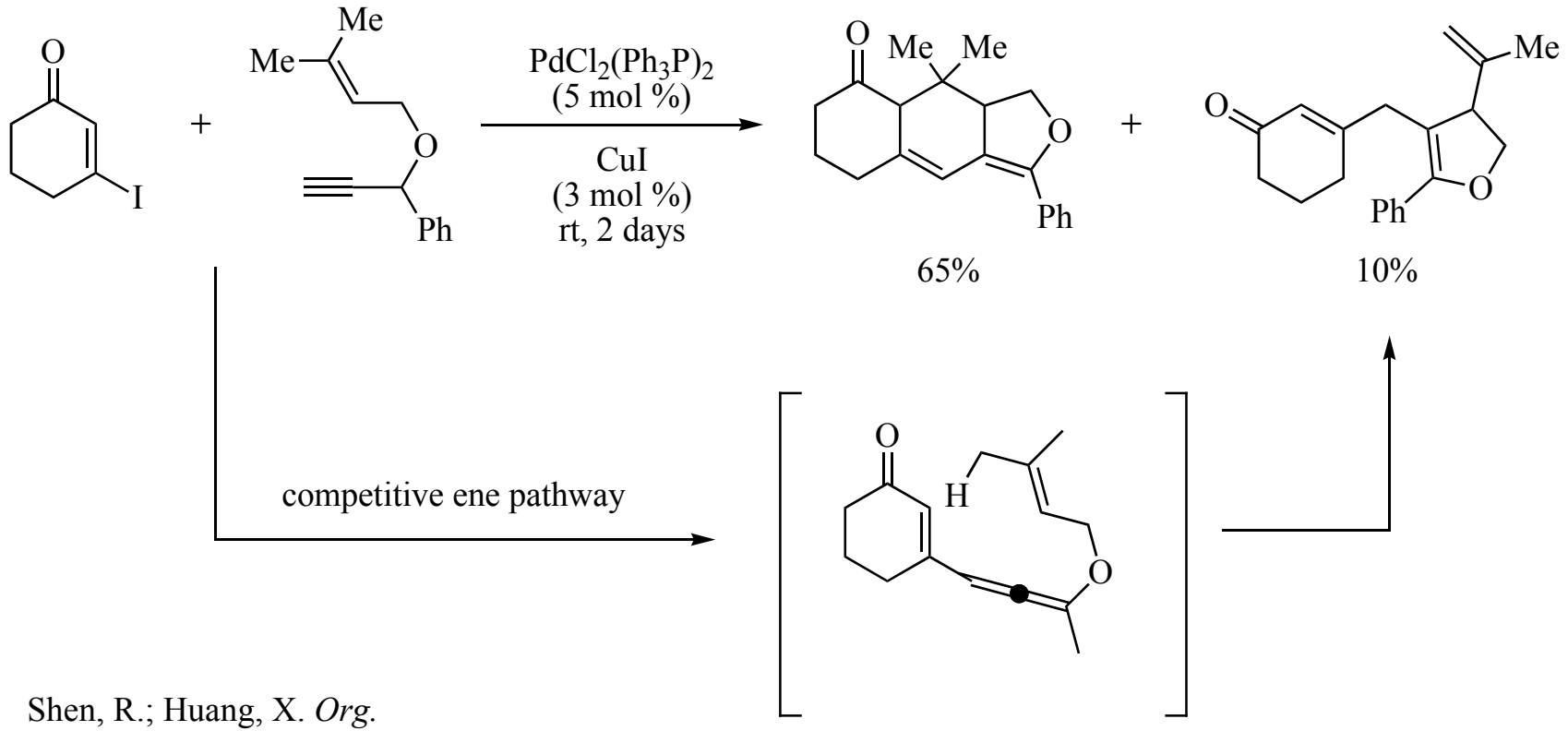
Shen, R.; Huang, X. *Org. Lett.* **2008**, ASAP

Proposed Mechanism



Shen, R.; Huang, X. *Org. Lett*. **2008**, ASAP

A competing side reaction



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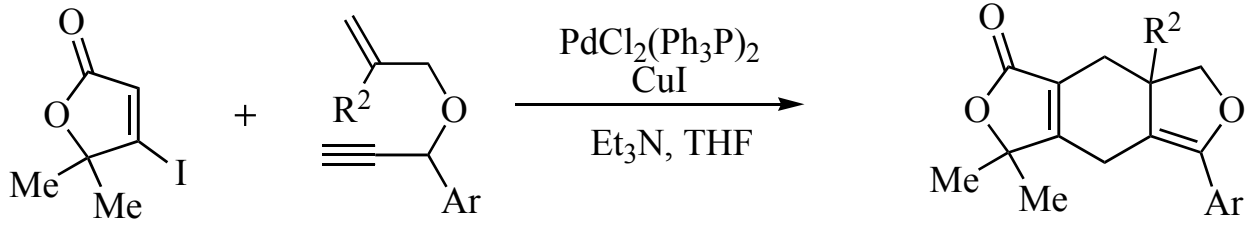
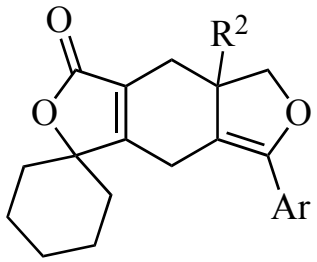
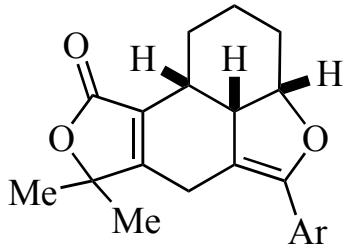
3-iodobuteneolides



8a: R^2 = H, Ar = Ph (76%)
8b: R^2 = H, Ar = p-FC_6H_4 (80%)
8c: R^2 = CH_3, Ar = 0-$MeOC_6H_4$ (68%)
8d: R^2 = H, Ar = 10-anthracene (61%)

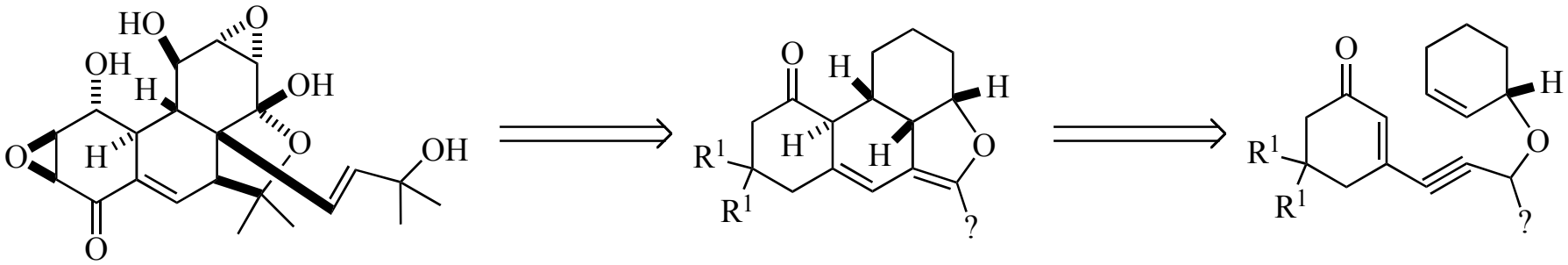


8e: Ar = 0-$MeOC_6H_4$ (60%)
8f: Ar = p-FC_6H_4 (81%)



8g: Ar = p-MeC_6H_4 (61%)

Additional characteristics to probe

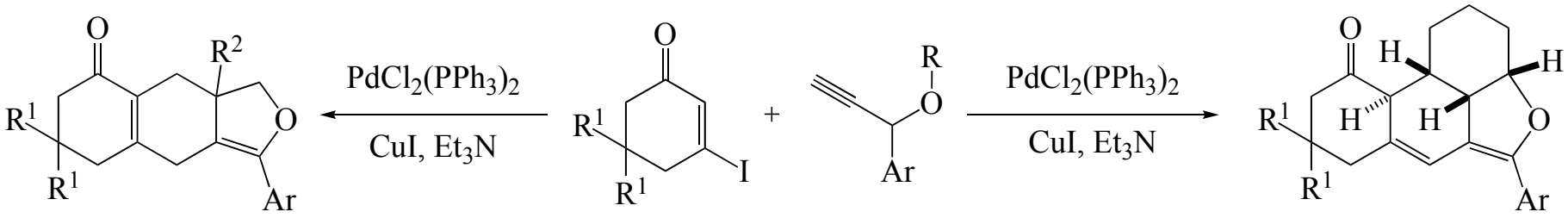


Panepophenanthrin

Sekizawa, R.; Ikeno, S.; Nakamura, H.; Naganawa, H.; Matsui, S.; Iinuma, H.; Takeuchi, T. *J. Nat. Prod.* **2002**, 65, 1491 - 1493

- Other functional groups located at the "Ar" position
- Structural complexity
- Substrate control on stereochemistry
- Other $Pd^{(0)}$ sources

Conclusion



Mild conditions to construct polycyclic ring systems containing a 2,3-dihydrofurnan moiety using a $Pd^{(0)}$ catalyst.

Construction of these polycyclic rings systems was achieved through a cascade process utilizing a Sonogashira coupling, allene formation through propargyl isomerization, and subsequent 4 + 2 cycloaddition.